HYDROBORATION OF 3-HEXYNE: FREE RADICALS WITH CATECHOLBORANE BUT STEREOSPECIFIC ADDITION OF DICHLOROBORANE[1]

Bonnie Schafman and Donald S. Matteson*

Department of Chemistry, Washington State University, Pullman, Washington 99164-4630 USA

Abstract. The reaction of catecholborane with 3-hexyne was found to produce more of the *trans*-addition product, catechol (*E*)-3-hexenyl-3-boronate, than the (*Z*)-isomer, a result totally inconsistent with the stereospecific *cis*-addition of catecholborane to internal alkynes previously reported. Reaction in the presence of azobis(isobutyronitrile), a free radical initiator, increased the proportion of (*E*)-isomer to >90%. Reaction in the presence of galvinoxyl, a free radical inhibitor, led to some increase in the amount of *cis*-addition product, but the *trans*-isomer still predominated. Attempted addition of dichloroborane to 3-hexyne using boron trichloride and triethylsilane was apparently superseded by boron trichloride addition, but the use of diethylsilane with boron trichloride resulted in efficient stereospecific *cis*-hydroboration. The resulting (*Z*)-3-hexenyl-3-boron dichloride was easily converted to the methyl ester with methanol. It was found that heat or radical catalysts would isomerize the (*Z*)-3-hexenyl-3-boronic ester to the (*E*)-isomer.

Introduction

Hydroboration was described long ago as an exclusively *syn* addition of boron and hydrogen to a carbon–carbon double or triple bond,[2] and the hydroboration of 4-octyne with catecholborane has been described as a totally routine and typical example.[3] Hydroborations of a wide variety of alkynes have been carried out under various conditions with all of the common hydroborating agents by a diversity of research groups, and no exceptions to the rule of stereospecific *syn* addition of boron and hydrogen have come to our attention.[4]

It was therefore a considerable surprise to observe that the reaction of catecholborane with 3-hexyne produced a mixture of catechol (*E*)-3-hexenyl-3-boronate and (*Z*)-3-hexenyl-3-boronate.

Materials and Methods

General Data. THF was freshly distilled from benzophenone ketyl. Other chemicals were reagent grade. ^{1}H-NMR and ^{13}C-NMR (75-MHz) spectra were recorded on a Bruker 300 MHz instrument.

Reaction of Catecholborane with 3-Hexyne. A. Without Radical Inhibitor. Catecholborane (21.33 mL, 24 g, 200 mmol) was added to 3-hexyne (22.68 mL, 16.4 g, 200 mmol) at room temperature. The reaction mixture immediately and spontaneously heated to reflux. The reaction was then cooled to 70 °C and refluxed for 3 h. The NMR spectrum showed a 4:1 ratio of catechol (*E*)-3-hexenyl-3-boronate (**1**) to (*Z*)-isomer (**2**) by integration of the vinylic hydrogen peaks at 6.7 ppm and 5.3 ppm respectively, with 98% conversion of the hexyne. In other runs with slight variations of these conditions, the proportion of (*E*)-isomer (**1**) varied from 74-87%. Subsequent work up with 200 mL of water yielded 1.612 g of precipitate, shown by ^{1}H-NMR to be catechol. The organic layer was shown by NMR to be exclusively (*E*)-boronic ester (16 g, 40%); 300 MHz ^{1}H-NMR ($CDCl_3$) δ 7.11 (m, 4, aromatic) 6.72 (t, 1, *J*=7.2), 2.37 (q, 2, *J*= 7.5), 2.26 (dt, 2,*J*=7.5), 1.08 (t, 3, *J* = 7.5), 1.07 (t, 3, *J*= 7.6); 75 MHz ^{13}C-NMR ($CDCl_3$) δ 150.8, 148.6, 122.35, 112.22, 21.9, 21.5, 14.9, 13.7; HRMS calcd for $C_{12}H_{15}BO_2$, 202.1165; found, 202.1146. In one instance, the (*Z*)-isomer was recovered as the boronic acid from the aqueous phase.

B. In the Presence of Galvinoxyl. Galvinoxyl (20 mg) was added to 3-hexyne (22.7 mL, 16.4, 200 mmol). Catecholborane (21.3 mL, 24 g, 200 mmol) was added dropwise over a period of 5 min. White fumes were noted. The solution became bright yellow upon the addition of the catecholborane. The reaction was stirred for 20 min at 40 °C, and then stirred at room temperature (25 °C) for one hour. The ^{1}H-NMR spectrum indicated 100% complete hydroboration with a 2:1 ratio of the (*E*)- to (*Z*)-isomer (1 to **2**). After 3 h a flocculent white precipitate had formed. The reaction was left at 20-25 °C for 48 h. The mixture was then treated with 20 mL of water and the resulting precipitate was collected but accidentally lost. The organic layer was shown by ^{1}H-NMR to be exclusively the (*E*)-isomer (1) (19.4 g, 48%). The *Z* isomer was not recovered.

C. In the Presence of Azobis(isobutyronitrile). A mixture of 3-hexyne (2.3 mL, 1.66 g, 20 mmol) and azobis(isobutyronitrile) (20 mg) was heated to 70 °C. Catecholborane (2.13 mL 2.49 g, 20 mmol, Aldrich) was then added dropwise over a period of 10 min. The mixture was refluxed at 70 °C for 3 h, then cooled and treated with 5 mL of distilled water. The organic layer was separated and shown by ^{1}H-NMR to be exclusively catechol (*E*)-3-hexenyl-3-boronate (4.13 g, 88%). In another run, the catecholborane was added faster, resulting in vigorous refluxing. ^{1}H NMR analysis of the crude product indicated a 10:1 ratio of catechol (*E*)- and (*Z*)-3-hexenyl-3-boronate, respectively, by integration of the vinylic peaks at δ 6.7 and 5.3. Aqueous work-up led to isolation of catechol (*E*)-3-hexenyl-3-boronate (1) (4 g), and (*Z*)-3-hexenyl-3-boronic acid was isolated together with catechol in a mixture (0.15) from the aqueous phase.

D. In the presence of AIBN at +70 °C. Catecholborane (2.13 mL, 2.6 g, 20 mmol) was added to 3-hexyne (2.3 mL, 1.6 g, 20 mmol) and AIBN (20 mg) which had been heated to 70 °C. The reaction temperature increased and the mixture boiled violently. The reaction was allowed to cool to 70 °C (20 min), and was subsequently refluxed for 4 additional h. NMR integration gives the *E*:*Z* ratio as 10:1. The reaction was cooled, then treated with 10 mL of water. A white precipitate resulted. The precipitate was filtered, and the resulting organic layer was shown by NMR to be exclusively catechol (*E*)-3-hexenyl-3-boronate (1) (4.1 g, 97.6%); 300 MHz ^{1}H-NMR ($CDCl_3$) δ 7.11 (m, 5, aromatic), 6.72 (t, 1. *J*=7.2), 2.37 (q, 2, *J*= 7.5), 2.26 (dt 2,*J*=7.5) ,1.08 (t, 3,*J* = 7.5), 1.07 (t, 3, *J*= 7.6). The *Z* isomer was recovered as boronic acid mixed with free catechol in the solid (0.15 g); 300 MHz ^{1}H-NMR ($CDCl_3$) δ 5.1 (t, 1), 2.36 (q, 2,*J*= 7.5), 2.29 (dt 2,*J*= 7.5), 1.08 (t, 6,*J*=7.5)

E. In the presence of AIBN at −40 °C 3-Hexyne (23 μL) was place in an NMR tube, which was subsequently capped and flushed with argon. AIBN (5 mg) was added and the solution was cooled to −40 °C. Catecholborane (21.3 μL) was added to the mixture at −40 °C. The reaction mixture was then photolyzed using a UV light source (UVGL-25 Mineralight lamp) for 8 hr. The reaction was then diluted with $CDCl_3$ (0.5 mL). ^{1}H-NMR analysis showed a nearly 1:1 ratio of (*E*) to (*Z*) isomers. There was also evidence of the migration of the vinylic bond to form catechol (*E/Z*)-2-hexenyl-3-boronate, characterized by an olefinic doublet (distorted by long-range coupling) located at 5.3 ppm and an olefinic quartet at 4.2 ppm.

Reaction of Boron Trichloride and Diethyisilane with 3-Hexyne. A mixture of 3-hexyne (11.33 mL, 8.215 g, 100 mmol) and diethyisilane (13 mL, 8.825 g, 100 mmol) was added dropwise to excess boron trichloride (12 mL, 11.71 g, 103 mmol) which had been condensed and cooled to −78 °C previously. The reaction was allowed to warm to 25 °C with the consequent evaporation of boron trichloride to yield a residue of *Z*-3-dichloroboryl-3-hexene (**4**); ^{1}H-NMR ($CDCl_3$) δ 7.1 (t, 1, $J = 6.9$), 2.4 + 2.3 (t + quintet, $J = 7.3$, 4), 0.97 (t, $J = 7.4$, 6); 75 MHz ^{13}C-NMR ($CDCl_3$) δ 160.3, 35.08, 14.6, 12.11, 6.03. When the excess boron trichloride had evaporated sufficiently, the reaction was quenched with a stoichiometric amount of methanol (8.75 mL, 7.11 g, 202 mmol). The major product was dimethyl *Z*-3-hexenyl-3-boronate (**5**) (15.4 g, 99%); 300 MHz ^{1}H-NMR($CDCl_3$) δ 5.7 (t, 1, $J = 6.9$), 3.6 (s, 6), 2.15 (q, 2, $J = 7.5$), 2.13 (q, 2, $J = 7.5$), 0.99 (t, 3, $J = 7.6$), 0.94 (t, 3, $J = 7.6$); 75 MHz ^{13}C-NMR($CDCl_3$) δ 140.2, 21.83, 14.0, 13.7, 6.2. Subsequent distillation attempts resulted in thermochemical isomerization of the double bond to the (*E*)-isomer (**6**), as shown by the appearance of the characteristic vinylic proton peak near δ 6.7 in the ^{1}H NMR spectrum, accompanied by some decomposition products.

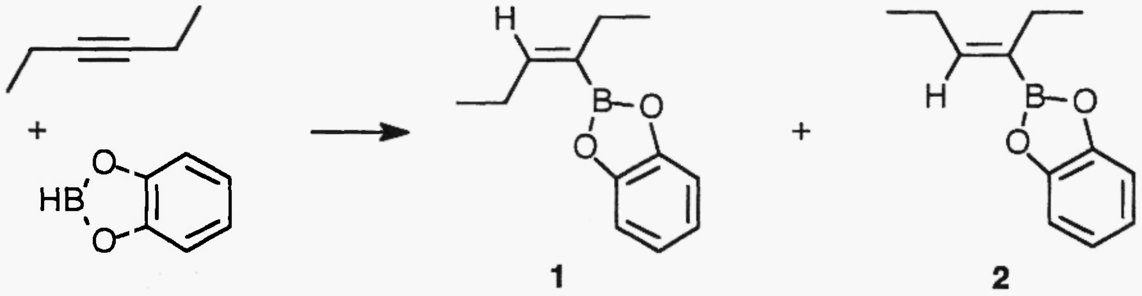
Reaction of Boron Trichloride and Triethylsilane with 3-Hexyne. A. Addition of Hexyne and Triethylsilane to 3-Hexyne. Boron trichloride (2.34 mL) was condensed at −78 °C. 3-Hexyne (1.9 mL) and triethysilane (2.3 mL) were mixed and then added over a period of ~10 min to the boron trichloride. The mixture fumed strongly during the addition. The reaction was quenched with a stoichiometric amount of methanol. It appeared that ~30% of the hexyne had been converted to dimethyl 4-chloro-3-hexenyl-3-boronate (**5**); ^{1}H-NMR($CDCl_3$) δ 3.6 (s, 4), 3.43 (s, 3), 2.39 (q, 2, $J = 7.2$), 2.13 (m, 5), 1.1 (m, 6) 0.90 (m, 5).

B. Addition of Boron Trichloride to Hexyne and Triethylsilane. *HAZARDOUS!* 3-Hexyne (20 mL, 305 mmol) and triethylsilane (25 mL, 305 mmol) were placed in a 500 mL three neck round bottom flask at −78 °C. To this solution was added boron trichloride (from a dry ice cooled addition funnel) at a slow rate. After 10 drops were added, the top of the addition funnel blew off, and a green flame erupted from the apparatus. The funnel was capped and the flame extinguished. The addition was completed in a dropwise fashion. The reaction was warmed to room temperature (approximately 25 °C) and the excess boron trichloride was vented through a water trap, leaving a residue that appeared to consist mainly of 3-chloro-4-dichloroboryl-3-hexene; ^{1}H-NMR ($CDCl_3$) δ 2.34 (q, 2, *J* = 7.5), 2.12 (q, 2,*J* = 7.5), 1.00 (t, 3, *J* = 7.5), 0.90 (t, 3, *J* = 7.6).

Reaction of Boron Trichloride with 3-Hexyne. 3-Hexyne (4.5 mL, 40 mmol) was cooled to −78 °C and boron trichloride (10 mL) was added in a dropwise fashion over five minutes. The mixture was allowed to warm to room temperature to evaporate the excess boron trichloride, leaving a residue that showed mainly alkyl CH in the ^{1}H NMR spectrum, plus some vinylic and allylic protons suggestive of ethyl- and other alkyl-substituted unsaturated units.

Results

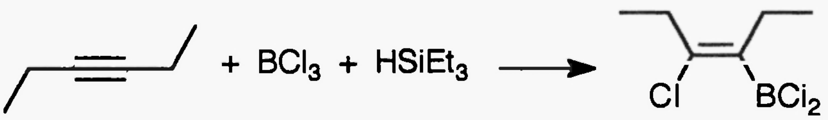
Hydroboration with catecholborane. Mixing catecholborane with 3-hexyne with no solvent resulted in an immediate exothermic reaction, with boiling of the 3-hexyne. The product ratio was ~80% catechol (*E*)-3-hexenyl-3-boronate (**1**) to 20% catechol (*Z*)-3-hexenyl-3-boronate (**2**). These isomers are readily distinguishable by the characteristic differing positions of their vinylic ^{1}H NMR peaks.[5]



Since it seemed likely that the production of the (*E*)-isomer (**1** had resulted from a free radical reaction, the reaction was tested in the presence of a radical inhibitor, galvinoxyl. The proportion of **1** was decreased to ~65-75%, in accord with the hypothesis of a radical mechanism for its production, but we did not find any way to make the reaction stereoselective for the (*Z*)-isomer (**2**).

Also in accord with the free radical hypothesis, the free radical initiator azobisisobutyronitrile led to enhanced production of the (*E*)-isomer **1** as ~90% of the product. It appeared that the (*Z*)-3-hexenyl-3-boronic ester (**2**) was more water soluble or more easily hydrolyzed than the (*E*)-isomer (**1**), as pure **1** was easily obtained in the ether phase when the reaction mixture was worked up in the usual way with water and ether.

Hydroboration with dichloroborane. Unsolvated dichloroborane generated in situ from a trialkylsilane or dialkylsilane has been found to be a rapid and efficient hydroborating agent.[6] We first tested 3-hexyne with triethylsilane and boron trichloride under several of the sets of conditions that had been found useful with other substrates. It appeared that the major product was that of addition of boron trichloride to the triple bond, 4-chloro-3-dichloroboryl-3-hexene (**3**), and that the hydroboration product was formed in very minor amounts. Evidence for structure **3** was provided by the two equal sets of ethyl group triplet plus quartet and the lack of vinyiic proton absorption in the ^{1}H NMR spectrum. When the reaction of 3-hexyne was repeated with boron trichloride alone, the NMR spectrum became very complex and suggested the presence of some **3** and perhaps isomers of **3** formed by double bond migration as minor components of a mixture of products containing mainly saturated hydrocarbon units.



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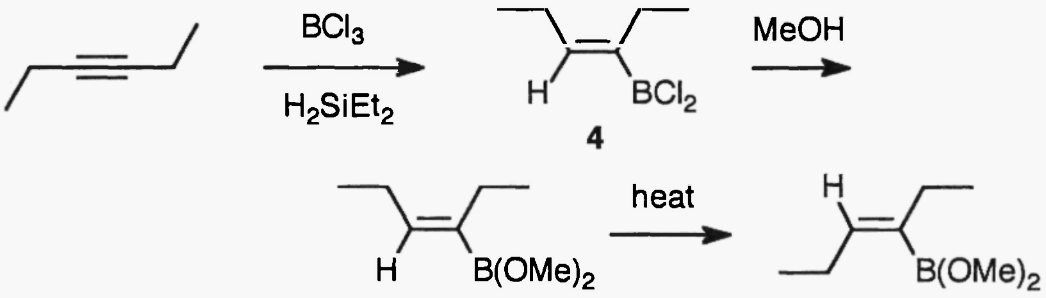
Hydroborations with diethylsilane and boron trichloride have been shown to be exceedingly rapid, even at –100 °C.[6] Accordingly, we tested the use of this reagent mixture and found that hydroboration became the major reaction. The resulting 3-dichloroboryl-3-hexene (**4**) and its methanolysis product dimethyl 3-hexenyl-3-boronate (**5**) appeared to be exclusively the (*Z*)-isomer. However, on attempted distillation, **5** was isomerized to the (*E*)-isomer (**6**).



5 **6**

Discussion

This work indicates that diethylsilane is a better reagent than triethylsilane for generating dichloroborane from boron trichloride in the presence of reagents that are particularly sensitive to boron trichloride. Evidently the rate of hydride/halide exchange is higher with the less sterically hindered diethylsilane, and the hydroboration step itself is exceedingly rapid. However, for most hydroborations, the less expensive triethylsilane works equally well.[6]

Our unexpected observation of nonstereospecific hydroboration with catecholborane does not necessarily imply that the original report[3] was inaccurate, as we were using commercial catecholborane rather than generating our own in situ reagent, which might behave differently. However, it certainly serves as a cautionary note regarding the possibility of such side reactions.

Our clear evidence that formation of the (*E*)-isomer in hydroboration with catecholborane is a radical process led us to consider the interesting possibility that the reaction might involve some sort of boryl radical intermediate in the mechanism for the hydroboration itself. However, the fact that dimethyl (*Z*)-3-hexenyl-3-boronate (**5**) can be isomerized thermally to dimethyl (*E*)-3-hexenyl-3-boronate (**6**) strongly implies that this is nothing more than a conventional radical catalyzed (*Z*)/(*E*) interconversion caused by radical initiating contaminants in the catecholborane, perhaps resulting from exposure of the reagent to atmospheric oxygen.

Finally, it may be noted that the ability to prepare either the (*Z*)-alkenylborane or the (*E*)-alkenylborane product from internal alkynes in a controlled manner, as discovered in this work, may have synthetic utility.

Acknowledgment

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